REMARKS/ARGUMENTS

The foregoing amendments in he specification and claims are of formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-47 were pending in this application and were rejected on various grounds. With this amendment, Claims 36-37 and 41-43 have been canceled without prejudice, Claims 28-35, 38-39 and 46 have been amended, and new Claims 48-54 have been added.

Claims 28-35, 38-40 and 44-54 are pending after entry of the instant amendment. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

The amendments to the specification, drawing and claims are fully supported by the specification and claims as originally filed and do not constitute new matter. In addition, new Claims 48-54 are fully supported by the specification as originally filed. Support for the amendment to Claims 48-54 can be found at least on p. 306, line 31 to p. 307, line 1 and on p. 107, lines 18-24, p. 107, line 37 to p. 108, line 1 and p. 280, lines 25-30 of the specification.

Specification

The specification has been amended to remove embedded hyperlink and/or other form of browser-executable code.

The specification has been amended to capitalize all of the trademarks and to include a proper trademark symbol, such as ™ or ®, following the trademark as requested by the Examiner. In addition, Applicants respectfully submit that generic terminology can be found immediately following or adjacent to each use of a trademark (*e.g.,* in a sentence preceding or following the use of the trademark). Accordingly, Applicants respectfully submit that every effort has been made to prevent use of trademarks in any manner which might adversely affect their validity as trademarks.

Drawing

Figure 74 has been amended to correct a typographical error. In Figure 74, under the section titled "Transmembrane domains:", the amino acid residue numbers "217-287" have been

amended to recite "271-287". Support for the amendment correcting the error can be found at least on p. 107, lines 29-31 and on p. 409, lines 25-26. A copy of the original Figure 74 showing the proposed change in red ink, together with a amended Figure 74 with the change made is enclosed herewith.

Priority

The Examiner stated that "this application is supported by the disclosure in application serial no. PCT/US00/04342, filed February 18, 2000 but is not supported by any of the earlier applications because no utility for the claimed polypeptide, PRO 1244, is disclosed in the earlier applications." Applicants rely on the endothelial cell proliferation assay (Example 136, Assay #8) and the mouse kidney mesangial cell proliferation assay (Example 145, Assay #92) for support of patentable utility.

The data for the endothelial cell proliferation assay was first disclosed in Example 55 of International Application Serial No. PCT/US99/28313 filed on November 30, 1999, the priority of which is claimed in the present application. Example 55 on page 171 of the PCT publication, WO 00/32221, corresponding to PCT application, PCT/US99/28313, disclosing the endothelial cell proliferation assay, is enclosed herewith.

The data for the mouse kidney mesangial cell proliferation assay was first disclosed in International Application Serial No. PCT/US00/04342 filed on February 18, 2000, the priority of which is claimed in the present application.

Furthermore, Applicants respectfully submit herewith Declarations by Dr. Goddard and Dr. Wood stating that the claimed PRO1244 polypeptide sequence and its encoding nucleic acid sequence were obtained prior to August 14, 1998.

Claim Rejections – 35 U.S.C. §101

Claims 46 is rejected under 35 U.S.C. §101, allegedly because the claimed invention is directed to non-statutory subject matter. The Examiner states that the claims are "drawn to host cells comprising a recombinant vector. The claim reads on cloned humans which are non-statutory subject matter."

Without acquiescing to the Examiner's position in the current rejection and solely in the interest of expediting prosecution in this case, Applicants have amended Claim 46 (and, as a consequence, Claim 47) to recite "an isolated host cell."

Applicants submit that the art-recognized meaning of "isolated" host cell is that the host cell has been identified and separated and/or recovered from a component of its natural environment. The support for selection and transformation of host cells can be found at least on p. 357 line 35 to p. 359, line 22 of the specification under Section 2 titled "Selection and Transformation of Host Cells." Therefore, the claimed host cells in Claim 46 are clearly distinguished over host cells in nature and the amendment to Claim 46 is supported by the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claim Rejections – 35 U.S.C. §112, Second Paragraph

Claims 28-33, 37, and 41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner noted that "[t]he limitation that the encoded protein comprises an 'extracellular domain' ... 'lacking its associated signal peptide' (Claim 28, part (d), for example) is indefinite[.]"

Since the terms "the extracellular domain" and "extracellular domain ... lacking its associated signal peptide" are no longer present in Claims 28-33 and 41 (and, as a consequence, those claims dependent from the same), the rejection is believed to be moot, and should be withdrawn.

Claim 37 has been cancelled without prejudice and hence, the rejection to this claim is believed to be moot, and should be withdrawn.

Claim 42 is rejected as "indefinite," since, according to the Examiner, the term "stringent conditions" is not defined in the specification. Examiner noted that "only examples of [stringent] conditions are presented on p. 306 and 307." Without acquiescing to the Examiner's position in the current rejection, Applicants submit that the cancellation of Claim 42 renders the rejection of this claim moot. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-32 and 41-47 are rejected under 35 U.S.C. §112, first paragraph, because "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims." The Examiner alleges that the specification "does not reasonably provide enablement for a polynucleotide that hybridizes to regions of SEQ ID NO: 129 or fragments of polynucleotides that are at least 10 nucleotides in length or a polynucleotide encoding a polypeptide not identical to at least the mature form of SEQ ID NO: 130 which does not have [the ACE growth stimulation activity or the mesangial cell proliferation induction activity]." (See Office Action, p. 4).

Without acquiescing to the Examiner's position in the current rejections, and without prejudice to further prosecution of the subject-matter in one or more continuation or divisional applications, Claims 28-32 (and, as a consequence, those claims dependent from the same) have been amended to recite a functional limitation wherein the claimed nucleic acid molecules encode polypeptides "capable of stimulating endothelial cell growth" or "capable of inducing proliferation of kidney mesangial cells." Furthermore, Claim 41 (and, as a consequence, those claims dependent from the same) has been amended to recite the conditions under which the hybridization of the nucleic acid molecules is to occur and to recite the hybridizing nucleic acid molecules to be "at least 50 contiguous nucleotides." Support for the amendment to Claim 41 can be found at least on p. 306, line 31 to p. 307, line 1 and on p. 107, lines 18-24 of the specification. Support for the amendment to Claim 43 can be found at least on p. 107, lines 18-24 of the specification.

Since the claims are now characterized by a combination of structural and functional features, any person of skill would know how to make and use the invention without undue experimentation based on the general knowledge in the art at the time the invention was made. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir.

1985) M.P.E.P. 2164.01.

Furthermore, the Examiner has admitted that the specification is "enabling for an isolated polypeptide having at least 80%, 85%, 90%, 95% or 99% nucleotide sequence identity to the polypeptide encoding a polypeptide comprising SEQ ID NO: 130 or the nucleic acid encoding the mature form of the polypeptide that hybridize to the full length of SEQ ID NO: 129, all of which encode a polypeptide that stimulates adrenal cortical capillary endothelial cell (ACE) growth and induces proliferation of kidney mesangial cells[.]" (See Office Action, page 4). In addition, the Examiner has also stated that the PRO1244 polypeptide "was shown to stimulate ACE growth (p.485, Example 136, Assay #8)" and to "induce proliferation of kidney mesangial cells (p. 505, Example 145, Assay #92)." (See Office Action, bottom of p. 4 to top of p. 5). Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim 42 has been cancelled without prejudice and hence, the rejection to this claim is believed to be moot, and should be withdrawn.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-37 and 41-47 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. The Examiner noted that in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Without acquiescing to the Examiner's position in the current rejections, and without prejudice to further prosecution of the subject-matter in one or more continuation or divisional applications, Claims 28-32 (and, as a consequence, those claims dependent from the same) have been amended to recite a functional limitation wherein the claimed nucleic acid molecules encode polypeptides "capable of stimulating endothelial cell growth" or "capable of inducing proliferation of kidney mesangial cells." Furthermore, Claim 41 (and, as a consequence, those claims dependent from the same) has been amended to recite the conditions under which the hybridization of the nucleic acid molecules is to occur and to recite the hybridizing nucleic acid molecules to be "at least 50 contiguous nucleotides." Support for the amendment to Claim 41 can be found at least on p. 306, line 31 to p. 307, line 1 and on p. 107, lines 18-24 of the

specification. Support for the amendment to Claim 43 can be found at least on p. 107, lines 18-24 of the specification.

Since the claimed genus is now characterized by a combination of structural and functional features, one skilled in the art at the effective priority date of the present application would be reasonably accepted that the inventors were in the possession of the invention as claimed. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim 42 has been cancelled without prejudice and hence, the rejection to this claim is believed to be moot, and should be withdrawn.

Claim Rejections – 35 U.S.C. §102

Claims 28-32 and 41-47 are rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent Application Publication No. 2003/0096951 (Jacobs *et al.*, effective filing date August 13, 1999, publication date May 22, 2003). Examiner alleges that SEQ ID NO: 3 encoding the polypeptide of SEQ ID NO: 4 disclosed in Jacobs *et al.* is 92.8% identical to SEQ ID NO: 129 of the present application.

Applicants thank Examiner Kapust for providing relevant pages from the priority document, provisional application 60/096,622 dated August 14, 1998, of U.S. Patent Publication No. 2003/0096951 disclosing SEQ ID NO: 4 in the publication.

In response, Applicants respectfully submit Declarations by Dr. Goddard and Dr. Wood, the consideration of which is respectfully requested.

Applicants simply need to disclose what is disclosed in the cited reference to support the priority claim

Applicants respectfully submit that the Declarations by Dr. Goddard and Dr. Wood ("Declarations") simply needs to provide a disclosure commensurate in scope with the disclosure in the priority document by Jacobs *et al.* to support the priority claim.

In order to remove a reference as a prior art, "[i]t is sufficient if [the affidavit under Patent Office Rule 131] shows that as much of the claimed invention as is taught in the reference has been reduced to practice by the [patentee] prior to the date of the reference." *In re* Stempel, 241

F.2d 755, 757 (1957). In *In re* Stempel, the patent applicant (Stempel) had claims directed to both (i) a particular genus of chemical compounds (the "generic" claim) and (ii) a single species of chemical compound that was encompassed within that genus (the "species" claim). In support of a rejection under 35 U.S.C. §102, the examiner cited against the application a prior art reference that disclosed the exact chemical compound recited in the "species" claim. In response to the rejection, the patent applicant filed a declaration under 37 C.F.R. §1.131 demonstrating that he had made that specific chemical compound prior to the effective date of the cited prior art reference. The Court found the applicant's 131 declaration effective for swearing behind the cited reference for purposes of both the "species" claim and the "genus" claim. Specifically, the Court stated in support of its decision that "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference." *Id.* at 759.

Furthermore, the Examiner is respectfully directed to *In re* Moore, 170 USPQ 260 (CCPA 1971), where the holding in *In re* Stempel was affirmed. In *In re* Moore, the patent applicant claimed a particular chemical compound in his patent application and the examiner cited against the applicant a prior art reference under 35 U.S.C. §102 rejection which disclosed the compound but did not disclose any specific utility for the compound. The patent applicant filed a declaration under 37 C.F.R. §1.131 demonstrating that he had made the claimed compound before the effective date of the cited prior art reference, even though he had not yet established a utility for that compound. On appeal, the Court indicated that the 131 declaration filed by the patent applicant was sufficient to remove the cited reference. The Court relied on the established "Stempel Doctrine" to support its decision, stating:

> An applicant need **not** be required to show [in a declaration under 37 C.F.R. §1.131] any more acts with regard to the subject matter claimed that can be carried out by one of ordinary skill in the pertinent art following the description contained in the reference ... the determination of a practical utility when one is not obvious need **not** have been accomplished prior to the date of a reference unless the reference also teaches how to use the compound it describes.

In re Moore, 170 USPQ at 267 (emphasis added).

Thus, *In re* Moore confirmed the holding in *In re* Stempel which states that in order to effectively remove a cited reference with a declaration under 37 C.F.R. §1.131, an applicant need only show that portion of his or her claimed invention that appears in the cited reference.

Accordingly, Applicants respectfully submit that the Declarations simply need to show possession of the polypeptide sequence and its encoding polynucleotide sequence disclosed in Jacobs *et al.* in order to remove Jacobs *et al.* as a prior art reference.

The cited Publication No. 2003/0096951 and the priority document 60/096,622 by Jacobs *et al.* disclose a polypeptide (SEQ ID NO: 4), which is identical to the PRO1244 polypeptide sequence (SEQ ID NO: 130) of the present application. However, the cited Publication No. 2003/0096951 does not teach that the polypeptide of SEQ ID NO: 4 is capable of stimulating adrenal cortical capillary endothelial cell (ACE) growth or inducing proliferation of mammalian kidney mesangial cells. Accordingly, Publication No. 2003/0096951 and the priority document merely disclose the amino acid sequence identical to the PRO1244 polypeptide and its encoding nucleic acid sequence that is 92.8% identical to SEQ ID NO: 129, but are devoid of any experimental data demonstrating the ACE growth stimulation activity or the mesangial cell proliferation induction activity as disclosed in the present application.

As shown in the Declarations, Applicants respectfully submit that Dr. Goddard and Dr. Wood, along with other inventors of the above-identified application, conceived and reduced to practice the PRO1244 polypeptide (SEQ ID NO: 130) and its encoding nucleic acid sequence (SEQ ID NO: 129) claimed in the present application in the United States prior to August 14, 1998.

As indicated in the Declarations and the brief description of Figure 73 of the present specification, the PRO1244 polypeptide is encoded by DNA 64883-1526.

Furthermore, as stated in the Declarations, the GSeqEdit database stores cloning and sequencing information for each PRO polypeptide and its encoding nucleic acid sequences according to its DNA number. Copies of the pages from the GSeqEdit database report (with the dates redacted) showing the cloning and sequencing information for the PRO1244 polypeptide sequences and its encoding nucleic acid sequence are attached to the Declarations as Exhibit A.

The GSeqEdit report shows the full length nucleic acid sequence for DNA-64883-1526 (identified as "DNA-64883") and the full length polypeptide sequence encoded by DNA 64883. As evidenced from the report and stated in the Declarations, both the nucleic acid and amino acid sequences shown in Exhibit A were obtained prior to August 14, 1998.

In addition, as stated in the Declarations, the DNA-64883 sequence shown in the GSeqEdit report is identical to the SEQ ID NO: 129 disclosed in the present application. The amino acid sequence shown in the GSeqEdit report is also identical to SEQ ID NO: 130 disclosed in the present application and to SEQ ID NO: 4 in Jacobs *et al.*

Accordingly, the attached Exhibit A clearly shows that Applicants were in possession of DNA-64883-1526 and the PRO1244 polypeptide encoded by DNA 64883-1526, as claimed in the present application, prior to August 14, 1998. Therefore, the Declarations clearly establish that the PRO1244 polypeptide and its encoding nucleic acid were conceived and reduced to practice prior to August 14, 1998.

Consequently, based on the teachings of *In re* Stempel and *In re* Moore, Applicants respectfully submit that Jacobs *et al.* is not prior art under 102(e) since its publication date and its effective filing date are after the effective priority date of the present application. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim 42 has been cancelled without prejudice and hence, the rejection to this claim is believed to be moot, and should be withdrawn.

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641**, referencing Attorney's Docket No. **39780-2830 P1C47**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 25, 2004

By: _____
Anna L. Barry (Reg. ~~No.~~ 51,436)

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